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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,132	11/15/2001	Brian A. Fox	00-62	5882

7590 03/09/2004

EXAMINER	
KAPUST, RACHEL B	

ART UNIT	PAPER NUMBER
1647	

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DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,132	FOX ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed December 15, 2003 has been entered. Applicants have cancelled claim 4. Claims 1-3, 5-8, and 18 are pending and under consideration.

Specification

The objections to the specification made in the Office Action dated July 1, 2003 are withdrawn in view of Applicants' comments and the amendment that removed the hyperlinks at pages 12, 40, and 42.

The use of the trademark HYBOND™ (p. 48), QIAQUICK™ (p. 49), NUCTRAP™ (p. 49), PEFABLOC™ (p. 50), DH10B™ (p. 52), BACTO™ (p. 52), QIAGEN™ (p. 52), ECL™ (p. 54), HYPERFILM™ (p. 54), GENE PULSER™ (p. 56), FAST-LINK™ (p. 56), and SEPHADEX™ (p. 57) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 18 is objected to for containing grammatical errors within the Markush group. The Markush group of 18(b) is lacking an "and" following "residues 35-412 of SEQ ID NO: 2;". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 1-3, 5-8, and 18 under 35 U.S.C. 101 is maintained for the reasons of record on p. 4-6 of the office action of paper no. 6.

Applicants argue on p. 7 of the response that they have disclosed tissue-specific expression of the claimed polypeptides and have identified a disease for which their presence would be diagnostic (*i.e.* kidney cancer and lung cancer). Applicants further argue the claimed polypeptides are specific markers of kidney cancer and lung cancer and thus have a specific and substantial utility as a disease marker. Applicants state the use of zcub5 as a target for cell labeling, *in vivo* imaging or diagnosis as disclosed on p. 36 are all specific uses. Applicants also argue the cited references are not relevant for the determination of patentability in view of the diagnostic utility disclosed by Applicants. In addition, Applicants argue zcub5 is a cell-surface protein, thus it provides a means of identifying, labeling, and isolating selected cell types, and provides a target for cell-specific delivery of diagnostic and therapeutic agents. Zcub5 can be used to generate anti-zcub5 antibodies, and these antibodies can be labeled and used for *in vivo* or *in vitro* labeling of cells, for in vivo imaging, and for other diagnostic procedures.

Applicants' arguments have been fully considered but have not been found persuasive. Applicants assert that the cited references are not relevant for the determination of patentability in view of the diagnostic utility disclosed by Applicants. The point of the cited references is that there is no well-established utility associated with the identification of zcub5 as related to neuropilins. As stated on p. 5 of office action paper no. 6, "the activity of neuropilin-1 and the mechanisms by which neuropilin-1 regulates angiogenesis still need to be elucidated". It is not known whether "binding of VEGF family members to neuropilin-1 or neuropilin-2 results in signal transduction in endothelial cells or in any other cell type" (p. 6 of paper no. 6). Thus, there is not a well-established utility for neuropilin-1 or proteins related to neuropilin-1. As such, neither a specific nor substantial utility is imparted on zcub5 just because it may be homologous to neuropilin-1.

Regarding Applicants' arguments that because zcub5 is a cell-surface protein, and it provides a means of identifying, labeling, and isolating selected cell types and that anti-zcub5 antibodies can be labeled and used for *in vivo* or *in vitro* labeling of cells, this does not provide a substantial utility for zcub5. First, these uses would be true for any cell-surface protein. Second, they are only useful in research to determine the function of

zcub5 itself and to distinguish it from other cell-surface proteins. There is no "specific benefit in currently available form" to be derived from such studies.

Similarly, although Applicants assert they have disclosed tissue-specific expression of the claimed polypeptides, tissue-specific expression such as that found Table 4 is not specific to the nucleic acid molecule encoding the claimed polypeptide. It does not depend on any characteristics of the nucleic acid molecule encoding zcub5 itself. Applicants argue that the presence of zcub5 would be diagnostic for kidney cancer or lung cancer, yet nowhere in the specification do Applicants state this. The only support for such a utility is found in Table 4. However, it is doubtful that one of skill in the art would be able to identify such a function for zcub5 from only reading the specification. For example, although Example 1 and Table 4 teach that zcub5 cDNA is found in human kidney cancer tissue and lung cancer tissue and is not found in the non-cancerous tissues, Example 3 teaches that mouse zcub5 cDNA is found in normal mouse kidney and lung tissue (p. 48). After reading the data presented in the specification, one of skill in the art would not have been able to determine that the presence of zcub5 in kidney tissue or lung tissue is diagnostic for cancer. Thus, Applicants have not provided a specific and substantial asserted utility for zcub5.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is dependent on a cancelled claim. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3, 5-8, and 18 under 35 U.S.C. 112, first paragraph, as lacking enablement because the claimed invention lacks utility is maintained for the reasons set forth above and on p. 6 of the office action of paper no. 9.

The rejection of claims 1-3, 5-8, and 18 under 35 U.S.C. 112, first paragraph, as lacking enablement is maintained for the reasons of record on pages 7-8 of the office action of paper no. 9.

Applicants argue that the recited regions of zcub5 are within the extracellular portion of the molecule, and as such they would be expected to be useful as immunogens for the preparation of antibodies useful in labeling cells expressing zcub5. Applicants further argue that the three-dimensional configuration of the zcub5 fragments is not important for an immunogen because antibodies recognize short, linear epitopes (p. 8).

Applicants' arguments have been fully considered but have not been found to be persuasive. Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the encoded protein which are tolerant to change (e.g., by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Specifically, Applicants are claiming polypeptides of unlimited length that comprise regions of the zcub5 polypeptide, and these polypeptides could have functions that are completely different from that of zcub5. There are no functional limitations placed on these variants of zcub5. In addition, because there is no utility for a zcub5 polypeptide, there would be not utility for an antibody that recognizes zcub5. Thus, fragments of zcub5 would not be useful as immunogens in the preparation of antibodies because the antibodies would have no utility.

Although the specification outlines art-recognized procedures for producing recombinant proteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the disclosed sequence as a starting point for further experimentation. Further, as stated above, there is no function ascribed to the encoded protein. There is no assay by which molecules could

be tested, and there is no other way that one of skill in the art could identify other molecules having the characteristics of zcub5; neither the activity nor other characteristic features required for it are set forth. What is provided is thus the idea for an invention, and the invitation to experiment to implement this invention, not the invention itself. Therefore, without further guidance, one of skill in the art would not be able to make and use biologically active variants of zucb5 (e.g., polypeptides of possibly 1800 amino acids in length comprising regions of 100 amino acids to 400 amino acids of zcub5).

The rejection of claims 1-3, 5-8, and 18 under 35 U.S.C. 112, first paragraph, as lacking sufficient written description is maintained for the reasons of record on pages 9-10 of the office action of paper no. 9.

Applicants argue the claimed polypeptides share the common feature of comprising epitopes within the extracellular region of the zcub5 protein.

Since, for the reasons set forth above and in the previous office action, there is no utility associated with the encoded polypeptide, one of skill in the art would not be able to determine the defining characteristics of the claimed genus. While the structural characteristics of one molecule are described, there is no known use and it therefore is not possible to identify molecules that have a common use, nor is it possible to identify what structural characteristics might be important for such a use. As discussed above, the claimed invention must have a use; see 35 U.S.C. 101. Thus, the essential features of the genus are not described and other members that share the same essential features cannot be identified. One of skill in the art would therefore not conclude that Applicant was in possession of the genus of zcub5 molecules, including proteins that comprise only a portion of the disclosed sequence, as broadly claimed.

Conclusion

NO CLAIMS ARE ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
3/1/04

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER